

CASE REPORT

Asthma Associated with the Use of Nitrofurantoin

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MANY drugs are known to be associated with allergic reactions, and such reactions to penicillin, aspirin and many other pharmaceuticals are commonly encountered. Reports of allergic reactions to nitrofurantoin (Furadantin) have been rare despite the widespread use of this drug in the treatment of urinary tract infections. A number of toxic reactions to the drug have been reported, but hypersensitivity or allergy to nitrofurantoin has been described in only a few instances. Such reactions have occurred in patients with and without previously recognized disorders.

In 1957 Fisk¹ reported the occurrence of an anaphylactoid reaction to nitrofurantoin. The patient had dyspnea but no pulmonary findings, and exhibited chest pain, headache, vomiting and a rash. In 1962, Israel and Diamond² reported a patient who had a reaction suggestive of Loeffler's syndrome. This case was characterized by the absence of previous allergic reactions, the development of pulmonary infiltrations, severe cough and asthmatic dyspnea, fever, malaise and eosinophilia. The attacks were severe and alarming but always subsided rapidly and the pulmonary infiltrations disappeared quickly. Three attacks followed the use of nitrofurantoin; the first two weeks after, the second 24 hours after, and the third eight hours after starting the drug. In this case the drug was prescribed for treatment of a urinary tract infection. The relationship of the attacks to the drug was demonstrated by a planned and deliberate administration of the drug, which resulted in reproduction of the symptoms and signs.

In 1963, Muir and Stanton³ reported the case of a physician who manifested acute fever, dyspnea, cough and pulmonary infiltrations following the use of nitrofurantoin. Recovery was rapid following withdrawal of the drug. The patient had a 20% eosinophilia in the peripheral blood. Khorsandian, Brener and Nodine⁴ reported a case with severe wheezing dyspnea, without pulmonary infiltrations and with associated urticaria, following the use of nitrofurantoin. They also recorded that the manufacturer of this product had records of eight cases of anaphylactoid reactions, which apparently included those mentioned above.

Robinson,⁵ in 1964, reported a severe asthmatic reaction in a woman with a previous history of asthma, following the use of nitrofurantoin. This patient also showed transient pulmonary infiltrations and eosinophilia.

In the past two years, I have observed two patients with an acute and rather alarming allergic type of reaction to nitrofurantoin (Furadantin).

CASE 1.—A 69-year-old woman had been treated at intervals for 17 years for mild recurrent allergic rhinitis and asthma and, occasionally, infective bronchitis. Her asthma had always been mild. She had been seen by various colleagues for a variety of other medical conditions, including recurrent lower urinary tract infections. On June 4, 1963, she was given nitrofurantoin, 100 mg. four times daily. Her urinary symptoms improved, but she developed a cough and slight dyspnea. On June 15, 1963, she became acutely ill with fever, severe cough, wheezing dyspnea and purulent sputum. Because she was thought to be suffering from bronchitis, she was given an antibiotic and improved rapidly. Coincidentally, she stopped using nitrofurantoin. On June 21, 1963, her urinary symptoms recurred and she resumed nitrofurantoin medication. Within an hour she became severely and alarmingly dyspneic and cyanotic. Marked signs of bronchial obstruction were noted and she responded to repeated injections of adrenaline. The following day she had recovered. No radiographic examination was carried out. A diagnosis of nitrofurantoin allergy was made and the drug was discontinued permanently.

Subsequently she had some minor episodes of asthma, as in the past easily relieved by oral medications, but no further severe or alarming attacks.

CASE 2.—A woman of 64 had been under my care for the past 15 years. She had suffered from asthma since the age of 45. She was sensitive to various environmental and seasonal allergens and also suffered from infectious asthma. She had also been known to be severely sensitive to aspirin and to penicillin and was wary of all drugs. Since 1951 she had been treated intermittently for episodes of lower urinary tract infection. Various sulfonamides had been used. Cortisone was started in 1954 because of intractable asthma and she did well. During that year renal calculi were demonstrated and in December 1955 a right nephrectomy was carried out. About that time her general care was assumed by her family physician and it is not known what medications were used.

In 1960 she was changed from cortisone to prednisone and was maintained on 5 mg. twice daily, with good control of her asthma and rhinitis. Early in November 1964, she had some recurrence of her urinary symptoms and nitrofurantoin was prescribed. After taking one tablet, she developed very severe asthma which subsided after several hours and she, quite properly, refused to take more of the drug. It is very likely that she had taken nitrofurantoin previously but we were unable to trace all of her previous medications. However, from time to time she had seen her family doctor because of urinary complaints and had been given various medications for this. Since stopping

nitrofurantoin she has remained well on her former dosage of prednisone, 5 mg. twice daily.

DISCUSSION

These two case histories are illustrative examples of probable nitrofurantoin sensitivity. While it could not be contended that allergy to nitrofurantoin has been proved in these cases, the clinical suspicion was sufficiently strong that these two patients will not be given nitrofurantoin in the future, since it seems reasonable to assume that the use of this drug would be very dangerous to them.

Less than a dozen cases of nitrofurantoin allergy have been reported to date, and in only one instance² was proof obtained by deliberate exhibition of the drug to a patient suspected of having such sensitivity.

While nitrofurantoin sensitivity seems to be rare, a number of cases may occur without being recognized. Everyone who looks after allergic people is aware that such persons sometimes manifest severe allergic reactions without the immediate cause being recognized. It is not unusual for patients to take medicines prescribed by another doctor, or obtained from a druggist, without the knowledge of the doctor who is treating the patient's allergic problems.

Patients who have experienced other drug reactions (e.g. our Case 2) are, of course, more alert to possible drug reactions and one has only to listen to them carefully. Case 1, a surgeon's wife, was accustomed to knowing what drugs she took and for what purpose.

Drug allergy is probably more common than is generally recognized. Many drugs are potential allergens and one must be constantly alert to this hazard. Those who use such drugs as nitrofurantoin frequently are unaware of the possibility of allergic reactions to this agent. Although published reports of allergic reactions to this drug are uncommon, it is desirable to draw attention to them when they occur.

Drug allergy is difficult to prove in a given instance because the only presently available

method is to give the suspected drug deliberately to a patient and observe his reactions. This may be very dangerous and seldom is justified. However, the patient may inadvertently carry out such a test (as in our Case 1), and one should be on the alert to recognize this phenomenon in such instances.

We do not know whether or not our patients had transient pulmonary infiltrations. Such infiltrations are not uncommon in acute asthma and must be distinguished from pneumonic infiltrations. The presence of fever and mucopurulent sputum and radiographic evidence of pulmonary infiltrations would naturally lead to a tentative diagnosis of pneumonia. When asthmatic dyspnea is present with signs of bronchial obstruction, the use of adrenaline may help to clarify the diagnosis. The withdrawal of all medications may then lead to rapid recovery. In our Case 1 the withdrawal of nitrofurantoin was fortuitous, and its reintroduction by the patient herself fortunately led to the correct diagnosis.

SUMMARY

Two cases of probable nitrofurantoin (Furadantin) allergy, with associated acute asthma, are presented. Allergy to nitrofurantoin is reported infrequently. The relevant literature on this subject is briefly reviewed. While nitrofurantoin sensitivity appears to be rare, it is perhaps more common than is appreciated. Although the etiologic role of this drug in the two cases described in this report has not been completely proved, this experience illustrates the importance of continued awareness of the hazard of drug sensitivity, particularly in relation to such commonly used drugs as nitrofurantoin.

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REFERENCES

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2. ISRAEL, H. L. AND DIAMOND, P.: *Ibid.*, 266: 1024, 1962.
3. MUIR, D. C. F. AND STANTON, J. A.: *Brit. Med. J.*, 1: 1072, 1963.
4. KHORSANDIAN, R., BRENER, E. M. AND NODINE, J. H.: *J. A. M. A.*, 184: 500, 1963.
5. ROBINSON, B. R.: *Ibid.*, 189: 239, 1964.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

WHY IS THE ATTENDANCE SO SMALL?

The number of names on the provincial medical register May 1, 1915, was two hundred and fifty-one. The average attendance at the New Brunswick Medical Society's meeting for the last eleven years, 1904-1914 inclusive, was forty-four. In the past this Society has had its sessions in the larger centres as St. John, Moncton, Fredericton, and St. Stephen. The attendance at each meeting has been chiefly from the place where the meeting was held and its vicinity. It is evident that the attendance is not a numerical representation of the province and that there is need of a stimulus to increase the attendance. It is left to the president and the secretary to arrange a program. They, I assure you,

have their difficulties. Request to be present and to take part in the program is sent to each registered practitioner. Why is the attendance so small? Apathy of the officers and failure to present an attractive program may be the cause but most of the fault is lack of interest. I have been told, among other reasons best passed over, that it is a waste of time to attend the meetings. Can we not make our meetings more attractive by the demonstration of interesting specimens in morbid anatomy, and the clinical side of the Society of a greater educational value through presentation of patients, particularly those illustrating rare and unusual forms of diseases?—G. Clowes Van Wart, *Canad. Med. Ass. J.*, 6: 5, 1916.